IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

NATERA, INC., Plaintiff, v. NEOGENOMICS LABORATORIES, INC., Defendant.	C.A. No. 1:23-CV-629

DEFENDANT NEOGENOMICS LABORATORIES, INC.'S OPPOSITION TO PLAINTIFF NATERA INC.'S MOTION FOR A PRELIMINARY INJUNCTION

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TABLE OF CONTENTS

Page(s)

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Rules

I. INTRODUCTION AND STATEMENT OF FACTS[1]

The Court should deny Natera's motion because it would remove a unique cancer testing option important to patients based on weak patent infringement claims.

RaDaR was independently developed by Inivata with its technological foundation published by Dr. Forshew in 2012. The industry recognizes its especially high sensitivity featuring 48 tumor-specific DNA variants and advanced bioinformatics. The FDA granted RaDaR a Breakthrough Device Designation in 2021. NeoGenomics Laboratories, Inc. ("NeoGenomics") paid over [redacted] for it.

NeoGenomics does not infringe because of important technological differences. There are also serious invalidity problems including obviousness, written description, inventorship, and ineligibility.

Natera's delay undermines its allegations of "clear" infringement and irreparable harm. RaDaR has been on the market since 2020. Natera states it believed RaDaR infringed the '035 Patent in December 2022, but cannot explain its eight-month delay asserting that patent, citing privilege.

Natera's excuse that it waited until the Medicare coverage decision fails. That ignores years of supposedly harmful RaDaR sales to biopharma; that Natera's decision to

[1] References to "Ex. __" cite the *Declaration of Derek Walter*. Emphasis is supplied unless otherwise indicated.

pursue an injunction predated the coverage decision; and, per industry experts, coverage decisions are not a major factor influencing market share.

Natera's irreparable harm argument fails because its CEO insisted that Natera "very rarely" sees competition and that meaningful competition is a long way off. Natera's expert testified that Natera's market domination is "durable" and agreed with analysts that Natera owns 74% of the market, while NeoGenomics has 3% and that this ***won't*** change much over the next 3-5 years.

Natera's main gripe appears to be that RaDaR is known for high sensitivity, which is grounded in analytic data. Natera has no false advertising claim in this case and thus its alleged harm from that is not cognizable.

Natera falls well short of proving that the Court should eliminate an important option of a highly sensitive and differentiated cancer test that is vital to patients, doctors and cancer researchers.

Thus, none of the preliminary injunction factors, much less all of them, favor Natera.

II. ARGUMENT

A preliminary injunction is an "extraordinary remedy." *Winter v. NRDC, Inc.*, 555 U.S. 7, 24 (2008). Plaintiff's burden is to prove all four preliminary injunction factors favor it. *Heart Imaging Technologies, LLC v. Merge Healthcare, Inc.*, 2013 WL 443125, at *3 (M.D.N.C. Aug. 14, 2013).

A. Natera Is Unlikely To Prevail

The Court should deny this motion if there is a "substantial question" regarding infringement or validity. *Trebro Inc. v. Firefly Equip.*, LLC, 748 F.3d 1159, 1165 (Fed. Cir. 2014).

1. NeoGenomics Does Not Infringe

a) The '454 Patent Is Not Infringed

There is no infringement if any claim requirement is missing. *CommScope Technologies LLC v. Dali Wireless Inc.*, 10 F.4th 1289, 1298 (Fed. Cir. 2021). Natera's motion included only literal infringement, not doctrine-of-equivalents. *Id.*

Natera asserts claims 1, 8 and 11. They require "performing targeted multiplex amplification to…obtain amplicons" and then "sequencing the amplicons to obtain sequence reads." D.I. 1-1 at 171:30. The claims state that the very "amplicons" generated by the amplification step in the claims are sequenced—not some other amplicons from a different and unclaimed step. They specify that "***the*** amplicons" are sequenced, which refers to the amplicons produced by the claimed "amplification" step. *Natera, Inc. v. ArcherDX, Inc.*, CA No. 20-125-GBW, D.I. 550 at 8 (D. Del. Feb. 6, 2023) ("[T]he definite article 'the' in conjunction with 'universal primer' recited in the second PCR refers to the initial antecedent phrase 'universal primer' as referred to in the first PCR."); *Harris Corp. v. Fed. Express Corp.*, 502 F. App'x 957, 963 (Fed. Cir. 2013) ("the" data in a claim step must refer to the specific data referred to in an earlier claim step "where, as here, the later instance refers to 'the' data and therefore begs for some antecedent basis").

While the claims require sequencing "the amplicons" that result from "targeted" amplification, the accused RaDaR process sequences amplicons that emerge from an amplification step that is different from the step that Natera contends satisfies the "targeted" amplification requirement. Specifically, RaDaR sequences amplicons from a subsequent universal, ***non-targeted*** amplification process. *See* Van Ness Decl. ¶¶ 84-87. Natera's own expert, Dr. Metzker, confirmed that this universal amplification step in RaDaR is ***not*** targeted. *See* Ex. 9 at 76:11-77:22 (The "second step is using common primers, not target-specific primers.")

Natera ignores this infringement problem. But Natera insisted to the Patent Office that the sequencing step must sequence the amplicons from the claimed amplification step ***without*** an intervening step. It did so for Natera's U.S. Patent No. 11,486,008 (the "'008 patent"), which shares with the '454 Patent the same parent applications, the same specification, title and includes similar claims in key respects. *See* Van Ness Decl. ¶ 79-80; D.I. 1-1; Ex. 1.

The Patent Office originally rejected the claims in the '008 Patent application. Ex. 2 at 4-8. The Patent Office based its obviousness rejection on a 2012 Forshew publication, dated before Natera's supposed invention. D.I. 13-7. The Forshew publication actually describes the process that is the basis for RaDaR. *See* Van Ness Decl. ¶¶ 117-118.

Similar to the '454 Patent, the rejected '008 claims required "performing multiplex targeted amplification to amplify at least 100 target loci…to obtain amplicons" and

"performing high-throughput sequencing to sequence the obtained amplicons to obtain sequence reads." Ex. 3 at 2. Natera distinguished Forshew (2012) by arguing that its claimed inventions required "performing high-throughput sequencing to ***sequence the amplicons obtained in the multiplex targeted amplification reaction*** to obtain sequence reads"—not the product of any subsequent amplification. Ex. 4 at 7 (emphasis in original). Natera asserted that Forshew "requires a subsequent and separate targeted amplification step…therefore Forshew's amplicons are not obtained from the alleged multiplex targeted amplification (i.e., '*limited-cycle pre-amplification step*')." *Id*. (emphasis in original).

Natera asserted in an Examiner interview including Natera inventor Bernard Zimmermann that "the highly accurate mutation detection obtained are ***due to lack of intermediate steps between the multiplex amplification and sequencing step***." Ex. 5 at 2.

Although the language of the amplification and sequencing limitations in the '454 Patent is not identical to the '008 claims, where claim language is not materially altered it can still shed light on the meaning of the claim step especially when it is used to distinguish prior art and describe the invention. *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 978-80 (Fed. Cir. 1999); *Juniper Networks, Inc. v. Palo Alto Networks, Inc.*, 15 F. Supp. 3d 499, 526 (D. Del. 2014) (applying earlier statements to similar claim language).

A broad construction of the '454 Patent claims that permits an intervening amplification step would be contrary to their plain wording and would eliminate the

distinction Natera drew between its purported invention and the prior art Forshew publication that is the basis for RaDaR.

Natera has territorial problems too. The "use of a patented method does not infringe unless 'each of the steps is performed within this country.'" *NTP, Inc. v. Rsch. In Motion*, 418 F.3d 1282, 1318 (Fed. Cir. 2005). One cannot "offer to sell" a method with steps performed overseas, as explained by Federal Circuit Judge Bryson. *F45 Training v. Body Fit Inc.*, 2022 WL 17177621, at *16 (D. Del. 2022). The claims require "detecting one or more of the tumor-specific SNV mutations," which involves bioinformatics steps processing raw data into results. RaDaR's bioinformatics steps are performed in Ireland using raw data to generate information for the doctor's reports, establishing non-infringement. *See* Sikri Decl. ¶¶ 48-51.

b) The '035 Patent Is Not Infringed

Natera asserts claims 1, 12, and 13. But none are infringed because they require the targeted amplification of ***already*** tagged DNA, which is not how RaDaR works. Van Ness Decl. ¶¶ 89-93. While RaDaR may use a targeted pre-amplification to generate tagged products, there are ***no*** subsequent targeted amplifications, a point Dr. Metzker confirmed. *See* Ex. 9 at 28:10-15, 77:10-12, 80:23-81:3.

Natera's motion, including the Metzker declaration, fails to address this problem. In deposition, Dr. Metzker pivoted to a belated argument that RaDaR's pre-amplification PCR step somehow satisfies both the tagging step and the post-tagging targeted

amplification step. *See* Ex. 9 at 88:18-22. Dr. Metzker attempts to break up RaDaR's single preamplifiction step into cycles, arguing that cycles involving the interaction of a single primer with an original cell-free DNA molecule are the claimed "tagging" step while only subsequent cycles are the required "targeted" amplification. *Id.* at 89:2-90:5, 90:15-91:6, 92:3-13; Van Ness Decl. ¶¶ 94-97. None of this is in Dr. Metzker's declaration, a point he could not credibly deny at deposition. *See* Ex. 9 at 91:20-24, 93:5-10, 94:10-95:22, 96:12-23, 98:13-99:8, 106:22-107:4. Nowhere does his declaration discuss the individual cycles of RaDaR's preamplification step. *See* D.I. 17 ¶¶ 87-101.

Regardless, as Dr. Van Ness explains, Dr. Metzker's belated theory defies the record and conflicts with his own testimony. *See* Van Ness Decl. ¶¶ 98-101. Most important, as Dr. Van Ness explains, the claim language proves conclusively that Dr. Metzker's theory is wrong. Claim 13, which depends from Claim 1, requires that the "tagging" comprises "amplifying the cell free DNA with a ***first primer*** comprising the first universal tail adaptor and a ***second primer*** comprising the second universal tail adaptor." By requiring the use of ***two*** primers (*i.e.*, a "first" and a "second"), claim 13 confirms that the claimed "tagging" process necessarily encompasses ***two*** cycles of PCR and cannot be limited to the interaction of ***one*** first primer with an original cell-free DNA molecule. *Id.* ¶¶ 100-101. Yet, as Dr. Metzker confirmed at deposition, limiting the claims to just a single primer interaction is essential to his untimely theory. *See* Ex. 9 at 107:6-108:1. This is but one of several logical flaws with Dr. Metzker's infringement opinion. *See id.* ¶¶ 102-108.

2. Invalidity

Once an alleged infringer "raises a substantial question concerning… validity," the patentee must prove the invalidity defense "lacks substantial merit." *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350-51 (Fed. Cir. 2001).

Natera's patent claims were drafted only recently to generate additional ammunition for its on-going litigation. Consequently, Natera's claims have become too broad and disassociated from the purported invention described in these patents, creating numerous invalidity problems addressed below.

Dr. Metzker fails to even explain what is actually inventive. Mr. Moshkevich, who manages this litigation, brags that these are "foundational patents" but could not describe what was inventive. D.I. 18 ¶ 16; Ex. 6 at 13:19-22. Natera's expert, Dr. Malani, undertook to understand "what was invented" for his patent nexus opinion but could not remember what was inventive. Ex. 7 at 118:19-24, 120:18-121:4.

a) Obviousness

A patent is invalid as obvious if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious. *See* 35 U.S.C. § 103; *KSR Co. v. Teleflex Inc.*, 550 U.S. 398, 399 (2007) ("A court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.").

Through its futile efforts to ensnare RaDaR, Natera has broadened the claims such that they now describe only routine and conventional steps found in the prior art and are dissociated from any purported invention disclosed in the patents.

Natera's obviousness problems for the '454 Patent, start with Forshew (2012). Natera and its expert actually cites Forshew to support their infringement claims against RaDaR. *See* D.I. 13 ¶ 56, 82; D.I. 17 ¶¶ 88-89, 100-01, 109-10, 113-14; Ex. 9 at 30:13–16. According to Dr. Metzker's infringement theory, Forshew discloses every key claim element. *See* Van Ness Decl. ¶ 117.

Any argument that Forshew does not disclose a sequencing depth of at least 50,000 per target locus is belied by Natera's and its experts' repeated assertions that increasing sequencing depth was conventional and easy to do in 2012. *See* Van Ness Decl. ¶¶ 145-149, 211-215, 338; *id.*, Ex. 10 at 26-27, Ex. 12 ¶¶ 211-215, Ex. 20 ¶ 119.

Natera may argue that the Patent Office considered Forshew. But Natera misled the Patent Office by arguing that Forshew did not include "multiplex" amplification. Van Ness Decl. ¶¶ 168-169; Ex. 8 at 9 ("Forshew deliberately resorted to parallel ***single-plex*** amplification."). Dr. Metzker now admits that "Forshew (2012) does describe multiplex PCR." Van Ness Decl. ¶ 169; *see* Ex. 9 at 65:15-18, 66:19-24. Natera also did not reveal its admissions that increasing sequencing depth was conventional. The Patent Office was misled about the technical teachings of Forshew. *See* Van Ness Decl. ¶¶ 170-176.

While Forshew invalidates the '454 patent, so too does Bashashati. *See id.* ¶¶ 177-220. Bashashati teaches a cancer monitoring approach based on identification of SNV mutations in tumors through "whole exome" sequencing, followed by targeted amplification of the tumor mutations from cell-free DNA and, finally, detection of mutations by sequencing. *See id*. As Dr. Van Ness explains, there is no meaningful difference between Bashashati and the alleged inventions of the '454 patent. *See, e.g.*, *id*. ¶¶ 195-99. Bashashati likewise expressly teaches the claimed sequencing depth of 50,000, confirming the obviousness of increasing sequencing depth. See *id*. ¶ 207.

The '035 Patent is also obvious. Before the supposed invention, Fluidigm sold "Access Array," which scientists could use to perform the multiplex amplification that Natera now asserts is central to its patent. Van Ness Decl. ¶ 222. Natera accuses Access Array multiplexing of infringement. *See id.* ¶¶ 95, 222.

A 2010 prior art publication by Kaper describes the use of Access Array to perform the process that Natera has attempted to claim. *See id.* ¶¶ 222-226; *id.*, Ex. 15. Dr. Kaper teaches the same multiplexing and renders the claims of the '035 Patent obvious and ARM-PCR does so too for similar reasons. *See* Van Ness Decl. ¶¶ 235-303; *id.*, Ex. 16 ¶ 32, Ex. 24 at 1520.

Any argument that Kaper does not specify cell free DNA fails. Such DNA was well-known by 2010 for use with cancer analyses and there is no special challenge

identified for its use in the claimed invention. Natera and its experts have admitted these points in the past. *See* Van Ness Decl. ¶¶ 241-248; *id.*, Ex. 7 ¶¶ 85-87, Ex. 20 ¶¶ 57-58.

Any argument Kaper only discloses 10-plex amplification fails. The '035 Patent itself acknowledges that "the general belief in the art is that multiplexing PCR for sequencing is limited to about 100 assays in the same well." D.I. 1-2 at 48:25-27. A skilled artisan would have found it obvious to perform multiplex amplification at least up to this supposed 100-plex limit. Moreover the prior art is filled with higher plexing than the claimed 25-plex. *See* Van Ness Decl. ¶¶ 264-269.

b) Written Description

The written description requirement requires that the "disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). This prevents patentees from claiming a broad genus of multiplex methods disassociated from what the patent describes as essential. *See, e.g.*, *Arthrex, Inc. v. Smith & Nephew, Inc.*, 35 F.4th 1328, 1342–44 (Fed. Cir. 2022) (claims to generic "eyelets" invalid where patent taught that "fixed aperture" eyelet was essential and criticized "flexible" eyelets); *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998).

Iitially, the claims of the '454 Patent refer to "whole ***genome*** sequencing" as part of the invention. However, the only reference to "whole genome sequencing" in the patent is an admitted error. Van Ness Decl. ¶¶ 385-386; Ex. 10 at 65:22-66:10. This is a written

description violation because the patent does not show that "whole genome sequencing" was possessed as part of the invention.

More broadly, the patents lack examples of the claimed processes. *See* Van Ness Decl. ¶¶ 418-426. Instead, the patents are directed to a mathematical scoring method to select the best primers for multiplex amplification without creating unwanted byproducts called primer-dimers. D.I. 1-2 at 54:46-50 ("At high multiplexing it is not possible to eliminate all spurious interactions, but it is ***essential*** to remove the primers or pairs of primers with the highest interaction scores in silico as they can dominate an entire reaction, greatly limiting amplification from intended targets."); D.I. 1-1 at 108:18-22 (same). The claims are disassociated from the described invention of reducing unwanted side products. *See* Van Ness Decl. ¶¶ 404-426.

c) Improper Inventorship

A patent is invalid if the correct inventors are not identified. *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1349-50 (Fed. Cir. 1998).

The claimed inventions of the '454 Patent are a collaboration between UCL (including Dr. Jamal-Hanjani) and Natera. The first step of the claims require "whole exome sequencing" which Dr. Jamal-Hanjani contributed to conception. Natera's corporate designee, Dr. Zimmerman, acknowledged that Example 13 was the only example corresponding to the claims and "whole exome sequencing." Ex. 10 at 64:5-11 ("we did not find others"). Example 13 is from the Hanjani Thesis. *See* Van Ness Decl. ¶¶ 394-

397. Correspondence from UCL produced by Natera recognizes Dr. Jamal-Hanjani's contribution. Ex. 11 at NAT-NEO-0888162 ("It would as such seem that Mariam should be named as an inventor on the patent application and the UCLB as a co-applicant" and "Example 13 corresponds to at thesis"); *cf.* Ex. 12. Natera's discovery argument to the Court that "NeoGenomics presents only a wildly speculative and unfounded story about alleged work of Dr. Jamal-Hanjani to case a cloud of doubt around inventorship," D.I. 55 at 19, is now proven to be far off base.

Dr. Zimmerman testified that the first experiment with Claim 1 method was "in the collaboration with Dr. Jamal-Hanjani." Ex. 10 at 80:17-23. He also admitted that the first "whole exome sequencing" step of the claims was performed by her. *Id.* 81:16-24. Dr. Zimmerman agreed Example 13 was a collaboration between Natera and her. *See id.* 87:18-25. Dr. Jamal-Hanjani should be an inventor, if there is one. *See* Van Ness Decl. ¶¶ 396-400.

Dr. Zimmerman argued that Natera supposedly "conceived" the claims before the collaboration. Ex. 10 (Zimmerman Tr.) at 104:6. But Natera identified April 2015 for its conception, which is ***after*** Dr. Jamal-Hanjani had contributed step one to the invention in 2014. Ex. 13 at 10; Van Ness Decl. ¶¶ 398-400. Natera provided this conception date in a supplemental interrogatory response after the Court ordered it to do so to avoid a "moving target" conception date. *See* D.I. 55 at 12-13; D.I. 60.

There is also a major inventorship problem with the '035 Patent. Natera supposedly "corrected inventorship" by removing five inventors and adding four. Ex. 14 at NAT-NEO-00002772–2775. Natera did not explain to the Patent Office the basis for this major reshuffle. After the Court Ordered Natera to respond "comprehensively" to this interrogatory on the substantive basis, *see* D.I. 60 at 2, Natera contended that its answer was privileged, Ex. 15 at 10-11. The Court observed: "Neither NeoGenomics nor the Court can have any confidence that Natera is not withholding relevant information based on these forfeited, waived, or overruled objections" and further suggested again that Natera "comprehensively answer[] the interrogatory." D.I. 82 at 5-6. Natera added little more. Ex. 16 at 2.

Many of the inventorship explanations appear dubious such as troubleshooting or vague description of generalized tasks. Ex. 15 at 12; Ex. 16 at 9.

Depositions of named and removed "inventors" are warranted. This is yet another substantial issue warranting denial of the motion.

d) §101

The parties' co-pending motion to dismiss briefing on §101 establishes substantial questions of invalidity. Natera's argument there that the Court cannot fully consider expert evidence relating to that defense will not apply to the merits stage and further shows that a substantial question is raised. Van Ness Decl. ¶¶ 312-340, 348-382.

B. Natera's Irreparable Harm Showing Fails

1. Natera Delayed

Delay "undercuts the urgency that forms the cornerstone of injunctive relief." *Quad/Tech, Inc. v. QI B.V.*, 701 F. Supp. 2d 644, 657 (E.D. Pa. 2010).

Natera significantly delayed. Natera claims its inventions date to 2011, but failed to claim them for nearly a decade. RaDaR has been commercially available for over three years for use with biopharmaceutical companies. *See* Sikri Decl. ¶ 11; D.I. 7 ¶ 46; D.I. 8-4 at 3; Ex. 7 at 34:18-35:4. Two years ago, Inivata publicly obtained FDA Breakthrough Device Designation for RaDaR. *See* D.I. 7-15 at 6. Shortly thereafter, Inivata began publicly announcing its RaDaR collaborations with biopharma. *See, e.g.*, Sikri Decl. ¶ 13. Natera has been aware of RaDaR's commercialization for years. *See* Sikri Decl. ¶¶ 11-15.

First, Natera sued Inivata for patent infringement in December 2022, but delayed suing ***NeoGenomics*** even though its irreparable harm expert admitted it was "well known" by October 2022 that "***NeoGenomics*** was commercializing the RaDaR test." Ex. 7 at 76:23-77:2; D.I. 11-9 at 5. Natera's Inivata complaint also admitted it knew RaDaR was sold "through" ***NeoGenomics***. *See* Ex. 17 ¶ 32.[2]

Second, for eight months Natera delayed alleging RaDaR infringed the '035 Patent. Although Natera states it had "reason to believe" RaDaR infringed on December 6, 2022,

[2] Inivata's motion to dismiss remains pending. *See* D.I. 6 at 5-6.

it contends its reason for the delay is privileged and thus should not be permitted to offer an excuse now. *See* Ex. 18 at 19.

Third, Natera did not allege irreparable harm in December 2022, even though it brought suit against RaDaR. *See* Ex. 17. Yet, Natera now alleges that RaDaR sales to biopharma that began years earlier cause irreparable harm and justify extraordinary relief. *See* D.I. 6 at 17-19. Natera's irreparable harm interrogatory response states [redacted] for example. *See* Ex. 19 at 10-11.

Natera's attempt to tie its "urgency" allegation to the late July 2023 Medicare decision fails.

First, Natera ignores years of RaDaR biopharma sales supposedly causing it irreparable harm. *See* Ex. 7 at 34:18–35:4, 76:23–2.

Second, Natera knew NeoGenomics was selling commercially for clinical use since at least March 2023 but waited until the end of July to file this motion. *See* Sikri Decl. ¶ 15.

Third, Natera apparently decided to bring this motion by the end of June ***before*** the coverage announcement. *See* Ex. 7 at 15:6-10, 20:1-5.

Fourth, Natera places way too much weight on a single coverage decision. Natera's own expert relies on a key Cowen analyst report, D.I. 12-23, which he describes as a "good report," that undermines Natera's position. Ex. 7 at 90:22-24. That report recently concluded that the quality of clinical evidence, NCCN guideline designation, and

turnaround times were the top three factors doctors considered when "choosing an MRD test vendor." Ex. 20 at NEOGEN00004211. Coverage decisions ranked sixth or seventh. *Id.* at NEOGEN00004241.

2. Natera's Lost Market Share Argument Fails

Potential lost sales alone do not demonstrate irreparable harm. *Abbott Lab'ys v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1348 (Fed. Cir. 2006) (agreeing "potential lost sales alone demonstrate manifest irreparable harm…would require a finding of irreparable harm to every manufacturer/patentee, regardless of circumstances"); *Impinj, Inc. v. NXP USA, Inc.*, No. 19-cv-03161-YGR, ECF No. 472, at 3 (N.D. Cal. Oct. 3, 2023) (in two-player market, defendant's "superior read sensitivity" did not cause plaintiff's alleged irreparable harm).

Natera has failed to make the requisite "clear showing" here.

First, the record belies Natera's allegation that RaDaR is "uniquely positioned to rapidly and substantially subvert Signatera's" market share. D.I. 6 at 11. Not only does Natera enjoy a "dominant" market position, but market analysts, Natera's expert, and Natera itself expect that dominance to continue. A key Cowen report, relied upon by Natera's own expert, concludes that Natera controlled 74% of the MRD assay market, making it the "dominant MRD vendor today" and projecting it would "remain so in the

future." Ex. 20 at NEOGEN00004215.[3] Natera's expert agrees that Natera "has a dominant market position" that is "durable," Ex. 7 at 24:14–25:5, 125:13–126:10, and further agreed with Cowen's current and future market share estimates, *id.* at 98:11–99:16. While Cowen projects Natera will lose a little market share, Guardant Health—not NeoGenomics—is expected to be the primary beneficiary. *See* Ex. 20 at NEOGEN00004210 (over next three to five years, Natera loses 7% but Guardant Health gains 6%, and in breast cancer, specifically, Natera loses 11% while Guardant picks up 11 points). Cowen projects NeoGenomics's market share will only increase from 3% to 5% in the next three to five years. *See id.*, -4215; Malackowski Decl. ¶¶ 47, 54-55. NeoGenomics's alleged infringement has not been shown to cause Natera to lose market share or its "first-mover" advantage. *See* D.I. 6 at 12–17; Malackowski Decl. ¶ 74.

Second, Natera's public statements—including ***during*** the pendency of this motion—demonstrate that Natera and NeoGenomics do not directly compete in the MRD market. Malackowski Decl. ¶¶ 56–57. On June 13, 2023, Natera's CEO stated "it's a very large market, so obviously there's a lot of room for competition," and Guardant Health is "really the only company we've actually seen in the field from the standpoint of MRD testing." Ex. 27 at NEOGEN00059562. Just a few weeks ago, Natera's CEO emphasized it does not see significant MRD competition. Ex. 21 at NEOGEN00018317 ("We very,

[3] Ex. 21 at NEOGEN00018317–18 (Natera's CEO, Steve Chapman, stating that Natera has "90-plus percent market share" and "there's been ***very limited competition***").

very rarely see any competitors in the field today. And I think in the vast majority of cases, if we see a competitor, it's Guardant and the tumor-naïve MRD testing."). Solomon Moshkevich, Natera's corporate representative, and Dr. Malani, Natera's expert did not disagree. *See* Ex. 6 at 66:5–17; Ex. 7 at 30:5–19.

Mr. Chapman also stated that for "the groups that are entering the space," such as NeoGenomics, "they've got a very long way to go to sort of get to a point where it's really part of the discussion from a physician standpoint." Ex. 21 at NEOGEN00018317.

Mr. Chapman's public statements also disprove Natera's allegation that tumor-informed and tumor-naïve MRD assays occupy different markets. Mr. Chapman stated that doctors draw no distinction between tumor-informed and tumor-naïve assays. *See id.* ("[T]he reality is, is that the investors talk a lot about other technologies, tumor-informed technologies and tumor-naïve technologies, but the doctors don't.").[4]

Third, Natera failed to show it would have secured NeoGenomics's biopharma contracts over the last three years. Many of those contracts were entered before Natera's patents issued. Sikri Decl. ¶¶ 13, 30–32, 34, 36, 39. Natera's expert on irreparable harm included no opinion supporting such harm in his declaration and could not identify any in

[4] Natera's [redacted] *See, e.g.*, Ex. 22 at NAT-NEO-00729506 [redacted] *see also* Ex. 23 at NAT-NEO-00864964 [redacted]

deposition. *See* D.I. 6 at 17–19; *see, e.g.*, Ex. 7 at 46:8–47:5, 48:23–49:5, 57:15–24 ("I cannot put my finger on any specific contract that was lost."). Likewise, in response to an interrogatory asking for the efforts Natera made to obtain lost contracts, it includes only vague efforts and does not describe any bids or concrete explanation for why it lost sales. Ex. 19 at 10-15.

Natera's corporate designee, Mr. Moshkevich, testified [redacted] *See* Ex. 6 at 110:2-10. Yet, he could not support Natera's position. For example, even though Natera claims that NeoGenomics's alleged infringement "deprived" Natera "of an opportunity to partner with Moderna for its PCV study in Melanoma," D.I. 6 at 18, the reality is that—even though [redacted]—Moderna had no interest in partnering with Natera on that project. Sikri Decl. ¶ 32. [redacted] *See* Ex. 6 at 126:7-127:7. Similarly, although Natera [redacted] *See* Ex. 6 at 110:6-112:5; Sikri Decl. ¶ 33. Natera does not know [redacted] *See* Ex. 6 at 123:23-124:3; Sikri Decl. ¶ 31. Natera does not claim [redacted]. *See* Ex. 6 at 128:22-129:2. Natera does not know [redacted] (*see id.* at 113:8-10),

[redacted] (*see id.*at 115:1-3),[5] or [redacted] (*see id.* at 125:23-25). Nor does Natera know [redacted] (*see id.* at 115:15-22), [redacted] (*see id.* at 116:21-23), or [redacted] (*see id.* at 122:16-123:4).

Natera's unsupported "beliefs" are plainly insufficient to support the extraordinary relief it requests and given the thinness of its discovery responses, it should not be heard to say anything more. *Well Cell Glob. LLC v. Calvit*, 2023 WL 6156082, at *3 (Fed. Cir. Sept. 21, 2023) (non-precedential) (district court abused its discretion by issuing preliminary injunction where movant's "irreparable harm allegations rested on unsubstantiated assertions").

Natera previously licensed the patent rights at issue here to Clarient, showing it can quantify the price of licensing its patents to a competitor. *See* Malackowski Decl. ¶¶ 78-81; *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1338 (Fed. Cir. 2012) (finding harm caused by alleged infringement to be quantifiable where patented product was licensed).

Natera claims NeoGenomics is "free-riding" on Natera's investments in obtaining coverage reimbursement determinations. *See* D.I. 6 at 17. Yet Natera's CEO recently said the exact opposite. *See* Ex. 24 at 5 ("The other thing that I think is important is that this

[5] Natera did not know [redacted] *See id.* at 119:7–24; *see also id.* at 120:18–22 (same for [redacted].

idea that you can just ride the reimbursement coattails of a company like Natera. That's proven actually to in fact not be true.").

3. Natera Is Not Suffering Reputational Harm

Natera caused its own loss of reputation and its attempt to blame NeoGenomics is unavailing. Natera has created its own tarnished reputation for Signatera among opinion leaders for high-sensitivity applications. RaDaR has better sensitivity data than Signatera.

Natera recognizes Professor Swanton of UCL as a "very influential" scientist who is a "very important person in the field." Ex.25 at 232:20–233:13, 254:25–255:19. Natera admitted that Professor Swanton's decision to stop working with Natera's Signatera test created a negative reputation for Natera's MRD technology. Ex. 26 at 549:19–550:5 (after Professor Swanton chose "different technology everybody started asking questions why what happened is there something wrong with Natera."). Natera acknowledges it lost Signatera business from Astra-Zeneca because of Professor Swanton's negative view. Ex. 25 at 255:20–256:4 ("I believe he was quite a influential in Natera not getting that"). Another major pharma company, Bristol Myers Squibb, also had a negative view of Signatera because of Professor Swanton's stature and steered away from Natera. Ex. 25 at 256:17–25 ("In the case of BMS, there seemed to be a tension, as I recall, from very early on because they were quite close with Charlie Swanton and he was not happy with Natera.").

Another influential MRD opinion leader, Dr. Nick Turner, recently critiqued Signatera's performance at a June 2023 American Society of Clinical Oncology conference. *See* Sikri Decl. ¶ 41. Dr. Turner's critique was pointedly at Signatera's clinical performance for breast cancer indications and had nothing to do with NeoGenomics and RaDaR. *See id.* Dr. Turner's critique was based on his own experience, which included substantial work with Signatera. *See id.*

NeoGenomics's Mr. Sikri confirms the views of the major industry luminaries that Signatera has a negative reputation for sensitivity and customer support. *See id.* ¶ 44. Numerous clinical research partners work with RaDaR in good part because of RaDaR's sensitivity. *See* Sikri Decl. ¶¶ 37-39.

As an example of this view, Dr. Beitsch, a prominent doctor who uses MRD cancer tests regularly, submits a letter explaining why the choice of an MRD cancer test with greater sensitivity such as RaDaR is important for patient care. *See* Ex. 32 at 2 ([redacted]

RaDaR's higher sensitivity is scientifically supported. RaDaR has an analytical sensitivity with a limit of detection of 0.001% variant allele fraction (VAF), meaning

RaDaR can detect 11 mutant haploid genomes among a background of 1,000,000 normal haploid genomes. Sikri Decl. ¶ 44. Signatera tracks only up to 16 tumor-specific variants per patient, and Signatera's limit of detection is 0.01% VAF, which is equivalent to 1 mutant haploid genome in a background of 10,000 normal haploid genomes. *Id.* This demonstrates a limit of detection that is up to ten times more sensitive than Signatera.

4. Lack of Nexus

A sufficient nexus between the alleged infringement and product sales is required. *Apple, Inc. v. Samsung Co.*, 678 F.3d 1314, 1323-24 (Fed. Cir. 2012). Natera relies on Dr. Malani to try to establish this, but as explained above, he did not even know what was supposedly inventive. Ex. 7 at 118:19-24, 120:18-121:4. There is insufficient nexus because RaDaR's sales are driven by the sensitivity that comes from RaDaR's 48 tumor-specific variants, and advanced bioinformatics, not Natera's patents. *See* Sikri Decl. ¶ 44.

C. The Balance Of Harms Disfavors A Preliminary Injunction

The balance of harms strongly disfavors an injunction. Natera has dominant control of the MRD market that its expert called "durable" and its CEO brags faces essentially no competition. If NeoGenomics were enjoined now, however, that would jeopardize its relatively small market share. Natera's irreparable harm expert testified that ***NeoGenomics*** would suffer irreparable harm if the Court granted this motion. *See* Ex. 7 at 145:1-146:2.

Eliminating NeoGenomics's MRD market share and disrupting its biopharma relationships would change the status quo, not preserve it. Courts have found the balance

of harms disfavors an injunction where the moving party has the majority market share. *See, e.g.*, *Waters Corp. v. Agilent Techs. Inc.*, 410 F. Supp. 3d 702, 717 (D. Del. 2019) ("The 'status quo' includes a 75-80% market share for Waters and 20-25% market share for InstantPC."); *Novozymes A/S v. Danisco A/S*, 2010 WL 3783682, at *10 (W.D. Wis. Sept. 24, 2010).

NeoGenomics invested approximately [redacted] to acquire Inivata to obtain the RaDaR technology and has invested [redacted] since. *See* Sikri Decl. ¶ 42. That investment in its unique and independently developed product weighs against an injunction. *Westinghouse Corp. v. Siemens Inc.*, 2018 WL 3655782, at *1 (D. Del. 2018).

D. The Public Interest Favors Patient Choice

The "focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." *Hybritech Inc. v. Abbott Lab'vs*, 849 F.2d 1446, 1458 (Fed. Cir. 1988)). In *Hybritech*, the Federal Circuit found the public interest favored availability of a cancer test. *Id.* The same conclusion is warranted on this record. *See, e.g.*, *Cordis Corp. v. Boston Scientific Corp.*, 99 F. App'x 928, 935 (Fed. Cir. 2004) (finding a "strong public interest support[ed] a broad choice [for a particular medical device]" where "the record contain[ed] evidence that some doctors prefer[red] the [defendant's medical device] over [plaintiff's]"); *Novo Nordisk A/S v. Pfizer Inc.*, 2006 WL 3714312, at *6-7 (S.D.N.Y. 2006); *Conceptus, Inc. v. Hologic, Inc.*, 2012 WL 44064, at *3-4 (N.D. Cal. Jan. 9, 2012);

While no test is good for all MRD indications, Mr. Sikri explains that some companies and doctors prefer RaDaR for particular uses because of its unique attributes such as high sensitivity. *See* Sikri Decl. ¶¶ 29-36, 44-47. NeoGenomics's contracts with biopharmaceutical companies and research partners demonstrate that choice. *See id.* ¶¶ 30-36, 39. Much of NeoGenomics's new business comes from sophisticated biopharma companies reaching out to NeoGenomics because of RaDaR's unique strengths and increased sensitivity. *Id*. ¶ 29.

Medical professionals rely on NeoGenomics's RaDaR because of its sensitivity and prefer choice in the marketplace for deciding patient care. *See* Ex. 28; Sikri Decl. ¶ 44.

Interfering with prospective trials would hurt the public interest, including patients, because of the need a continuity of care and access to therapies, and would hurt on-going cancer research because a transition to a diagnostic with a different assay is normally impractical. *See* Sikri Decl. ¶¶ 30-34, 37, 39, 42-43.

III. CONCLUSION

For the foregoing reasons, NeoGenomics respectfully requests that the Court deny Natera's Motion for a Preliminary Injunction.

This the 19th day of October 2023

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CERTIFICATE OF WORD COUNT

The undersigned counsel hereby certifies that this brief complies with the word count limitations of Local Rule 7.3(d).

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CERTIFICATE OF SERVICE

I hereby certify that on October 19, 2023, I electronically filed the foregoing **DEFENDANT NEOGENOMICS LABORATORIES, INC.'S OPPOSITION TO PLAINTIFF NATERA'S MOTION FOR A PRELIMINARY INJUNCTION** with the Clerk of Court using the CM/ECF system.

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